

## REMARKS

The rejection of all of the now-pending claims under §102 and/of §103 in view of Kamb, U.S. Patent No. 5,807,679 is respectfully traversed because the Office is not at liberty to disregard the contrary teachings of the applied prior art. Specifically, the Office states, at paragraph 8 of the Final Office Action, that the "unique sequence" as described by Kamb meets Applicant's recited limitation of "a region of fixed nucleotide sequence identical or complementary to a consensus sequence of interest." See clause (a) of Claim 1. The Office goes on to note, at paragraph 9 of the Final Office Action, that Kamb uses his disclosed approach "to increase dramatically the rate of completely sequencing very large fragments of DNA." Emphasis added.

This rejection is traversed because the object of the present invention is not "complete sequencing" as taught by Kam. In distinct contrast, the aim and object of the present invention is specific sequencing of only those areas of interest. (This is a positive limitation of Claim 1, which requires, in (c) that the area bounded by the first and second primers be "specifically" amplified.) The "unique sequences" of Kamb are entirely arbitrary, random, thoughtless, etc. The "unique sequences" of Kamb are not designed (as is the fixed portion of Applicant's primers) to amplify a pre-selected area of the target nucleic acid. As noted earlier, Kamb's primers bind randomly to the target. The "unique sequence" of Kamb is included solely to provide a known hybridization primer site for subsequent sequencing.

And this point is absolutely critical: there is no motivation to modify Kamb's approach to arrive at Applicant's claimed method because Kamb's entire stated purpose is to sequence the entire DNA target, not selected portions of it. On this point there can be no dispute:

The present invention is directed to determining rapidly the complete sequence of large fragments of DNA. (Kamb, column 4, line 51, emphasis added.)

If Kamb's approach were modified so that his "unique sequences" bound only to desired consensus regions of the target DNA, the complete sequence could not, and would not be amplified and thus could not be sequenced. The utility of Kamb's approach would be utterly destroyed. It is well settled that where a proposed modification destroys the utility of

the method described in the applied prior art, the rejection is improper. Thus, the Kamb patent neither anticipates or renders obvious the present claims because Kamb's amplification is purposefully designed to be non-specific, using random primers, under low-stringency "sloppy" conditions. Kamb's amplification is not specific as required by the present claims.

In point of fact, it is the degenerate portions of Kamb's primers that control where the primers hybridize, not the unique portion. Kamb's primers hybridize randomly throughout the target DNA. These primers are then amplified, thus creating islands. Because the amplified islands then include the "unique sequence" from the first round of amplification, the islands can be extended using the "unique sequence" as a starting point to extend amplification into unknown portions of the target (using standard PCR with a primer fully complementary to the "unique sequence"). In this fashion, the islands are linked to form an entire continent (so to speak). Kamb purposefully runs the initial amplification under low stringency conditions so that the resulting "sloppiness" generates single-banded, but wholly random, amplification products. See the paragraph in Kamb at column 5, lines 27-50.

There is absolutely nothing "specific" about Kamb's approach. And making it specific, as required by Applicant's claims, destroys the stated utility of Kamb's approach. To function, Kamb first creates islands of known sequence, that are then linked via standard PCR to sequence the entire target.

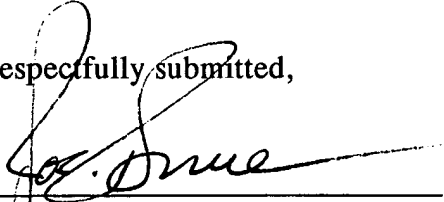
But in Applicant's view, sequencing the entire target is usually a waste of time. Instead, Applicant's claimed invention aims to sequence only the important parts of the target, those areas that flank a consensus sequence of interest. This approach is wholly distinct from Kamb's approach because Applicant's method does not seek to sequence the entire target, but only to amplify specifically those portions flanked by the first and second primers, primers which are purposefully designed to bind specifically to the target only at regions of interest.

Applicants thus submit that the continued rejection in view of the Kamb patent is clearly improper. Withdrawal of the same is respectfully requested.

### CONCLUSION

Applicant respectfully submits that the application is now in condition for allowance.  
Early notification of such action is earnestly solicited.

Respectfully submitted,

  
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